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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,405	11/17/2003	Allan L. Goldstein	2600-105	2020

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EXAMINER	
GUPTA, ANISH	
ART UNIT	**PAPER NUMBER**
1654	

NOTIFICATION DATE	DELIVERY MODE
01/16/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/714,405	GOLDSTEIN ET AL.	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *8,9 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10,11 and 13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 8/30/06, 2/22/06, 5/6/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-7, 10, 11 and 13-15, with the species of thymosin beta 4 in the reply filed on 8-2-07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 8-9 and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group II and III, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7-30-07.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Goldstein et al. (US5578570).

The claims are drawn to composition comprising of thymosin-β-4.

Goldstein et al. teaches that Tβ4 may be formulated in a conventional manner for administration by any suitable route. Suitable routes of administration include, but are not limited to, oral, rectal, nasal, topical, vaginal, and parenteral (including subcutaneous, intramuscular,

intravenous and intradermal) (see col. 3, lines 1-7). Formulations suitable for topical administration include lozenges comprising Tβ4 in a flavored basis, usually sucrose and acacia or tragacanth; pastilles comprising Tβ4 in an inert basis such as gelatin and glycerin, or sucrose and acacia; and mouthwashes comprising Tβ4 to be administered in a suitable liquid carrier. Formulations suitable for topical administration to the skin may be presented as ointments, creams, gels and pastes comprising Tβ4 and a pharmaceutically acceptable carrier, or may utilize a transdermal patch containing the ingredient to be administered (see col. 3, lines 33-43). Thus, it would have been obvious to formulate Tβ4 into a pharmaceutical formulation for topical purpose for the purposes of prompting wound healing.

While the reference may not disclose promotion, healing or prevention of blisters, sores and skin degeneration associated with Epidermolysis Bullosa, it has been held that the granting of the patent drawn to a composition cannot be based on a new use for the composition. See In Re Hack, 114 USPQ 161, 163 (CCPA 1957). The recitation of a new intended use for an old product does not make a claim to that old product patentable. In re Spada, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990) ("The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from prior art, can not impart patentability to claims to the known composition."); In re Pearson, 181USPQ 641, 644 (CCPA 1974) (intended use of an old composition does not render composition claim patentable); In re Benner, 82 USPQ 49, 53 (CCPA 1949) ("no provision has been made in the patent statutes for granting a patent upon an old product based solely upon discovery of a new use for such product"). In In re Zierden, 162 USPQ 102, 104 (CCPA 1969), one of the claim at issue was drawn to a "composition for removing and preventing alluvium deposits in water systems consisting essentially of insoluble potassium metaphosphate, solublizing agent therefor and a compatible dispersing agent." Zierden, at 103. Appellants argued

that the prior art at issue did not disclose or suggest that the composition of the prior art could be utilized to prevent alluvium deposition, as well as calcium carbonate deposition, from industrial waters. Zierden at 103. The U.S. Court of Customs and Patent Appeals maintained the prior art rejection under 102 and stated that "A mere statement of a new use for an otherwise old or obvious composition cannot render a claim to the composition patentable" Zierden at 104. The Court further stated, *citing* In re Lemin, 104 USPQ 273 (964), that the "difference over the prior at must be more substantial than a statement of intended use" and the composition of the prior art would be exactly the same whether the user were told to use it for the claimed purpose or the purpose disclosed in the prior art. Zierden at 104. Thus, since the prior art teaches the composition, the claimed limitations have been taught and the reference, thus, anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-7, 10-11, and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pierce et al (US5965530) and Roseeuw et al. (Medline abstract) in view of Malinda et al. (FASEB) and Frohm et al. (Eur. J. Biochem) and Goldstein et al. (US5578570).

The claims are drawn to a method of treating or preventing blisters, sores, skin dengenration associated with Epidermolysis Bullosa comprising administering a thymosin beta 4.

The reference of Pierce et al. teach generally Epidermolysis bullosa is a defect in adherence of the epidermis to the underlying dermis, resulting in frequent open, painful blisters which can cause severe morbidity. Accelerated reepithelialization of these lesions, would result in less risk of infection, diminished pain, and less wound care (see col. 2, lines 35-41). Roseeuw et al. Teaches that in epidermolysis bullosa, any therapy that improves wound healing would be beneficial for patients (see abstract). The difference between the reference and the instant application is that the reference does not specifically teach the use of thymosin-β-4 (Tβ4).

However, Malinda et al. Teach that Tβ4 interacts with G-actin and is through to be a important mediator in cell proliferation (see abstract). The reference demonstrates that Tβ4 acts as a chemoattractant, stimulating directional HUVEC migration (see page 476). In a wound closure

assay, accelerated wound closure was observed using Tβ4. The results indicated that migration was enhanced when cells were presented with uniform concentration of Tβ4 (see page 477). The reference concludes that the Tβ4 is an important factor in angiogenesis and suggested that it is involved to some extent in blood vessel formation. The formation of blood vessels is also important part of wound healing (see page 480). Tβ4 has been identified as a major constituent of wound and blister fluids and is proposed that it could play a major role in wound healing (see Frohm et al. and page 480 in Malinda et al.). As blood vessel are an essential early response to wounding, increased neovascularization resulting form Tβ4, one of ordinary skill in the art would conclude that the Tβ4 would be beneficial to wound healing.

Therefore, it would have been obvious to one of ordinary skill in the art to use Tβ4 in the treatment of blisters and sores in Epidermolysis bullosa. One or ordinary skill in the art would have been motivated to do so because in a wound closure assay, accelerated wound closure was observed using Tβ4 and As blood vessel are an essential early response to wounding, increased neovascularization resulting form Tβ4, one of ordinary skill in the art would conclude that the Tβ4 would be beneficial to wound healing. Furthermore, one would desired to use wound healing agents and there would have been a reasonable expectation of success that using wound healing agents is a beneficial treatment method for blisters or sores because the art teaches that accelerated reepithelialization of these lesions, result in less risk of infection, diminished pain, and less wound care and any therapy that improves wound healing is beneficial for patients with Epidermolysis bullosa.

Finally, the reference of Goldstein et al. teaches that Tβ4 may be formulated in a conventional manner for administration by any suitable route. Suitable routes of administration include, but are not limited to, oral, rectal, nasal, topical, vaginal, and parenteral (including

subcutaneous, intramuscular, intravenous and intradermal) (see col. 3, lines 1-7). Formulations suitable for topical administration include lozenges comprising Tβ4 in a flavored basis, usually sucrose and acacia or tragacanth; pastilles comprising Tβ4 in an inert basis such as gelatin and glycerin, or sucrose and acacia; and mouthwashes comprising Tβ4 to be administered in a suitable liquid carrier. Formulations suitable for topical administration to the skin may be presented as ointments, creams, gels and pastes comprising Tβ4 and a pharmaceutically acceptable carrier, or may utilize a transdermal patch containing the ingredient to be administered (see col. 3, lines 33-43). Thus, it would have been obvious to formulate Tβ4 into a pharmaceutical formulation for topical purpose for the purposes of prompting wound healing.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 13-15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 7,268,118. Although the conflicting

claims are not identical, they are not patentably distinct from each other because of the following reasons.

The claims are drawn to composition comprising of thymosin-β-4.

The US patent claims a composition comprising a polypeptide comprising amino acid sequence LKKTET [SEQ ID NO:1] or a conservative variant thereof, the composition further comprising a carrier for application to a surface of human body, wherein said carrier is for application to an external surface of said body or to an internal surface of said body, the composition comprising a gel, cream, paste, lotion, spray, suspension, dispersion, salve, hydrogel or ointment, wherein said polypeptide is gelsolin, vitamin D binding protein (DBP), profilin, cofilin, depactin, DnaseI, villin, fragmin, severin, capping protein, beta- actinin, acumentin, TB4, TB4ala, TB9, TB10, TB11, TB12, TB13, TB14, or TB15 , wherein said polypeptide is at a concentration in said carrier of at least about 0.01 ng/ml, and up to about 60 micrograms per 300 microliter (see claim 1). The US patent specifically claims the use of Tβ4 in the composition (see claim 12). The difference between the US patent and the instant claims is that the US patent does not specifically claim using Tβ4 for the promotion, healing or prevention of blisters, sores and skin degeneration associated with Epidermolysis Bullosa.

However, it has been held that the granting of the patent drawn to a composition cannot be based on a new use for the composition. See In Re Hack, 114 USPQ 161, 163 (CCPA 1957). The recitation of a new intended use for an old product does not make a claim to that old product patentable. In re Spada, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990) ("The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from prior art, can not impart patentability to claims to the known composition."); In re Pearson, 181USPQ 641, 644 (CCPA 1974) (intended use of an old composition does not render composition

claim patentable); In re Benner, 82 USPQ 49, 53 (CCPA 1949) ("no provision has been made in the patent statutes for granting a patent upon an old product based solely upon discovery of a new use for such product"). In In re Zierden, 162 USPQ 102, 104 (CCPA 1969), one of the claim at issue was drawn to a "composition for removing and preventing alluvium deposits in water systems consisting essentially of insoluble potassium metaphosphate, solublizing agent therefor and a compatible dispersing agent." Zierden, at 103. Appellants argued that the prior art at issue did not disclose or suggest that the composition of the prior art could be utilized to prevent alluvium deposition, as well as calcium carbonate deposition, from industrial waters. Zierden at 103. The U.S. Court of Customs and Patent Appeals maintained the prior art rejection under 102 and stated that "A mere statement of a new use for an otherwise old or obvious composition cannot render a claim to the composition patentable" Zierden at 104. The Court further stated, *citing* In re Lemin, 104 USPQ 273 (964), that the "difference over the prior at must be more substantial than a statement of intended use" and the composition of the prior art would be exactly the same whether the user were told to use it for the claimed purpose or the purpose disclosed in the prior art. Zierden at 104. Thus, since the US patent claims the same composition, the claimed limitations have been meet and the US patented claims are not patentably distinct from the claimed invention.

5. The reference of Marini (US6821524) has been cited as being pertinent to Applicants disclosure.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach

the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (571) 272-0562. The fax phone number of this group is (571)-273-8300.

10/30/07

Anish Gupta
Patent Examiner